Paper No. 17

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ROBERT F. BAUGH, LISA M. LIM, JULIE S. JOHNSTON,
and JOHN G. RIVERA

Appeal No. 2000-1906
Application 09/063,338

ON BRIEF

Before WINTERS, ROBINSON, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

An oral hearing in this case was scheduled for November 27, 2001. Upon reviewing the case, however, we have determined that an oral hearing will not be necessary and we render the following decision based on the record.

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-66. Claims 1, 17, 29, 41, and 53 are representative and read as follows:

1. A method of producing an autologous bioadhesive sealant from a single whole blood sample, comprising:

forming an inactive platelet rich plasma from said whole blood sample;

dividing said inactive platelet rich plasma into a first and a second portion;

reactivating said first portion of said inactive platelet rich plasma to form a clot;

triturating said clot to obtain a serum comprising autologous thrombin from said reactivated first portion; and

mixing said serum with said second portion of said inactive platelet rich plasma.

17. A method of producing an autologous bioadhesive sealant from a single whole blood sample, comprising:

forming an inactive platelet rich plasma and an inactive platelet poor plasma from said whole blood sample;

reactivating said inactive platelet rich plasma to form a clot;

triturating said clot to obtain a serum comprising autologous thrombin; and

mixing said serum with said platelet poor plasma.

29. A method of producing an autologous bioadhesive sealant from a single whole blood sample, comprising:

forming an inactive platelet poor plasma from said whole blood sample;

dividing said inactive platelet poor plasma into a first and a second portion;

reactivating said first portion of said inactive platelet poor plasma to form a clot;

triturating said clot to obtain a serum comprising autologous thrombin; and

mixing said serum with said second portion of said inactive platelet poor plasma.

41. A method of producing an autologous bioadhesive sealant from a single whole blood sample, comprising:

forming an inactive platelet rich plasma and an inactive platelet poor sample from said whole blood sample;

reactivating said inactive platelet poor plasma to form a clot;

triturating said clot to obtain a serum comprising autologous thrombin; and

mixing said serum with said platelet rich plasma.

53. A method of producing an autologous bioadhesive sealant from a single whole blood sample, comprising;

forming an inactive platelet rich plasma from said whole blood sample;

dividing said inactive platelet rich plasma into a first and a second portion;

adding human recombinant thromboplastin to said first platelet rich plasma portion to produce thrombin; and

combining said thrombin with said second portion of said inactive platelet rich plasma.

The examiner relies on the following references:

Antanavich et al. (Antanavich '007)	5,585,007	Dec. 17, 1996
Antanavich et al. (Antanavich '662)	5,788,662	Aug. 04, 1998
Hirsch et al. (Hirsh)	5,643,192	Jul. 01, 1997
Cochrum	5,510,102	Apr. 23, 1996
Barrow et al. (Barrow)	5,391,380	Feb. 21, 1995

Marieb, "Human Anatomy and Physiology," 2nd ed., Benjamin/Cummings Publishing Co., pp. 594-596 (1992)

Suzuki M et al. (Suzuki), "Clinical application of the fibrin adhesive," Otolaryngology, Vol. 56, No. 11, pp. 949-953 (1984)

Claims 1-66 stand rejected under 35 U.S.C. § 103 as obvious over Antanavich '007, Antanavich '662, Hirsh, Cochrum, Barrow, and Suzuki. We reverse.

Background

"[F]ibrin glue is a relatively new technological advance which duplicates the biological process of the final stage of blood coagulation." Specification, page 2. Fibrin glue is made by mixing fibrinogen with thrombin; the mixture forms a clot which can be used to control bleeding during surgery in cases where ordinary sutures cannot be used or where the patient suffers from a coagulation disorder. Id. Fibrin glue is used in Europe but has not been approved by the U.S. Food and Drug Administration, because fibrinogen concentrate or thrombin prepared from pooled blood donors carries a risk of transmitting viruses. Id.

The specification discloses a method for making fibrin glue autologously, i.e., based on components derived from the patient to be treated with the fibrin glue. The disclosed method comprises

> forming a platelet rich plasma or platelet poor plasma containing an anticoagulant. The platelet rich plasma or platelet poor plasma is then divided into two portions and the first portion is restored so that it can coagulate thus forming a clot. The clot is then triturated and the resulting serum is collected. The bioadhesive sealant composition is then prepared by combining a defined volume of the second portion of platelet rich plasma or platelet poor plasma with a sufficient volume of serum causing the fibrinogen in the second portion of platelet rich plasma or platelet poor plasma to be converted to fibrin which then solidifies in the form of a gel.

Specification, page 6.

Discussion

The claims are directed to various permutations of the basic method described above. For example, claim 1 is directed to a method in which the platelet-rich plasma fraction is divided and one portion is treated so as to activate the enzymatic clotting factors present in it, then the clot is removed and the activated clotting factors are combined with the rest of the platelet-rich plasma fraction. Claim 29 is directed to the same method, but using the platelet-poor plasma fraction instead. In claim 17, the platelet-rich plasma fraction is activated, then mixed with the platelet-poor plasma fraction. In claim 42, the platelet-poor plasma fraction is activated, then mixed with the platelet-rich plasma fraction. The method of claim 53 is similar to that of claim 1 but requires use of recombinant thromboplastin.

Even though the claims are directed to several different methods, the examiner treated them as defining a single invention.

> The claims are drawn to methods of producing autologous bioadhesive sealants from a single whole blood sample where inactive platelet rich plasma (iPRP) is obtained from whole blood. This iPRP is divided into two portions. The first portion is "reactivated", or in fact activated, since it was never activated, i.e., had its clotting cascade enzymes activated. Upon activation, the iPRP sample clots. From this clotted composition, the serum is obtained, which contains activated clotting enzymes such as thrombin, and this serum is mixed with the second iPRP portion. This combination now forms the sealant.

Examiner's Answer, page 5. The examiner's summary of the claimed method does not acknowledge the differences in the methods defined by, e.g., claims 17, 29, and 42.

The examiner rejected all of the claims over the combined teachings of Antanavich,[1] Hirsh, Cochrum, Barrow, and Suzuki. After reviewing the teachings of the references, the examiner concluded that

> it would have been obvious to one of ordinary skill in the art at the time the invention was made to produce an autologous bioadhesive sealant by withdrawing sufficient amount of autologous blood to prepare both the platelet rich plasma component and the thrombin component at the same time. . . . It further would have been merely a matter of saving time and resources to withdraw the blood and reduce it all to platelet rich plasma prior to separation for formation of the two components of the adhesive as it is clear from the prior art the platelet rich plasma would contain the thrombin (per the teaching of Hirsch [sic]) upon activation of the second portion of platelet rich plasma. . . . As it is well known from the teachings of the prior art taken as a whole, autologous proteins are always preferred to preclude issues of viral contamination and immune reactions to allogeneic proteins.

Examiner's Answer, page 8 (emphasis in original).

"In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant." In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). "The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art. Both the suggestion and expectation of success must be founded in the prior art, not in the applicant's disclosure." In re Dow Chem. Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988) (citations omitted).

[1] The examiner cited both Antanavich patents in the statement of rejection. However, the patents

After reviewing the record, we agree with Appellants that the examiner has not met her burden of showing prima facie obviousness. The cited references come closest to suggesting the process defined in appealed claim 1, i.e., a process in which a platelet-rich plasma fraction is made, then a portion of that fraction is treated to activate the endogenous clotting factors, and the activated clotting factors are mixed with the remaining platelet-rich plasma fraction to produce a fibrin glue.

Specifically, Antanavich discloses using a platelet-rich plasma concentrate as the source of fibrinogen in fibrin glue (column 12, lines 15-17), and both Antanavich and Hirsh disclose using thrombin to cause the fibrinogen to polymerize (Antanavich, column 12, line 17; Hirsh, column 2, lines 44-51). In addition, Hirsh teaches the advantage of using autologous thrombin in fibrin glue (column 1, lines 28-40). Hirsh also teaches deriving autologous thrombin from the part of the blood that is left over after fibrinogen is removed (column 2, lines 13-43). Finally, Antanavich teaches that using platelet-rich plasma concentrate in place of Hirsh's cryoprecipitated fibrinogen is advantageous because it is quicker (column 2, lines 10-26; column 11, lines 57-60). Thus, these references would have suggested a fibrin glue comprising autologous platelet-rich plasma concentrate, and autologous thrombin derived from what is left of the blood sample after the platelet-rich plasma is removed.[2]

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appear to have identical disclosures and the examiner did not make clear why she considered both to be necessary. For simplicity, we will cite to only one of the patents (5,585,007).

[2] Cochrum, Barrow, and Suzuki add nothing particularly relevant to claim 1.

These disclosures, however, fall short of showing the prima facie obviousness of the method of claim 1. The method defined in claim 1 requires first making a platelet-rich plasma fraction, then treating a portion of it to activate clotting factors, and using the activated portion as a source of thrombin. The cited references would not have suggested this series of process steps to those of ordinary skill in the art. Specifically, the references do not suggest using the same blood fraction as a source of both fibrinogen and thrombin in fibrin glue. At best, the references would have suggested using one fraction of a blood sample as a source of fibrinogen and another fraction of the same sample as a source of thrombin. For example, based on Hirsh, those skilled in the art may have found it obvious to use Antanavich's platelet-rich plasma concentrate as a source of fibrinogen and to use red and white blood cells as a source of thrombin.[3] That, however, is not the method of the instant claims.

The examiner argues that it "would have been merely a matter of saving time and resources to withdraw the blood and reduce it all to platelet rich plasma prior to separation for formation of the two components of the adhesive." Examiner's Answer, page 8. This argument is questionable on its face, since the examiner does not explain how reducing an entire blood sample to platelet rich plasma would "sav[e] time and resources." Even leaving that aside, however, the examiner's argument does not save the rejection because it presumes that those skilled in the art would have found it obvious to obtain both components of the

[3] Antanavich's platelet-rich plasma is made by removing red and white blood cells from whole blood. See column 12, lines 25-27 ("[P]latelet-rich plasma is separated from cells when

adhesive from the same fraction of a blood sample, a position that is not supported by the prior art.

With respect to the other methods defined in the claims, the prior art is even further from supporting a prima facie case of obviousness. Each of claims 17, 29, and 42 require the use of platelet-poor plasma as the source of either the fibrinogen or the clotting factors in the fibrin glue. The instant specification teaches that the platelet-poor fraction is produced by centrifuging a blood sample at low speed, removing the platelet-rich fraction, then re-centrifuging at high speed to precipitate the red and white blood cells. See pages 9-10. None of the references cited by the examiner disclose such a platelet-poor plasma fraction, nor do they suggest using one to make fibrin glue.

centrifugal force causes red and white cells to lodge irreversibly in a first separator."); see also column 12, line 53 to column 13, line 19.

Summary

We reverse the rejection on appeal because the references relied on by the examiner do not support a prima facie case of obviousness under 35 U.S.C. § 103.

REVERSED

Sherman D. Winters	)
Administrative Patent Judge	)
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	) BOARD OF PATENT
Douglas W. Robinson	)
Administrative Patent Judge	) APPEALS AND
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	) INTERFERENCES
	)
Eric Grimes	)
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